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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,669	11/27/2001	Ann-Kristin Karlsson	06275-160002	1605

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EXAMINER
MAIER, LEIGH C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/993,669	Karlsson
Examiner	**Art Unit**
L igh Mai r	1623

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *3, 4, 6, 8-12, 14, and 30-48* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *3, 4, 6, 8-12, 14, and 30-48* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2, 4

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Status of the Claims

Claims 1, 2, 5, 7, 13, and 15-29 have been canceled. Claims 3, 4, 6, 8-12, 14, 30, and 31 have been amended. Claims 32-48 have been added. Claims 3, 4, 6, 8-12, 14, 30, and 31-48 are pending.

Priority

Acknowledgment is made of applicant's claim for foriegn priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/230,781, filed on January 29, 1999.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

Claims 10 and 11 are objected to as not being proper dependent claims. A properly dependent claim is construed to incorporate by reference all the limitations of the particular

claim, claim 8, from which it depends. Claim 8 comprises the limitation of "*dry* finely divided particles." (Emphasis added)

Regarding claim 10, the claim appears to contemplate the use of additives that clearly conflict with the limitation of "dry finely divided particles." See, for example, "agents rendering the suspension isotonic."

Regarding claim 11, the claim recites a concentration in units (mg/ml) indicating a fluid composition, conflicting with the "dry" limitation in claim 8.

Claim 9 also recites a number of additives. However, this claim is *not* objected to. The claim is presumed to be properly dependent and limited to additives that would be consistent with the "dry" limitation of claim 8.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, 8-12, 30-34, 36-44, and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 3, 8, and 39 recite "glucocorticosteroids." The specification presents a non-limiting group of compounds that Applicant considers to be glucocorticosteroids. See page

4. However, in the art, compounds in this list are alternately called simply "steroids" (See ILLUM, page 168, under "Experimental") or "corticosteroids." (See BUSSEY, Table IV.) Given this, it is not clear that one of ordinary skill would be apprised of the metes and bounds of the particular group of compounds - that is what would be included and what would be excluded. The claims are thus rendered vague and indefinite.

Further regarding these claims, the claims recite "a glucocorticosteroid or ester, acetal, or salt thereof wherein the glucocorticosteroid . . . comprises an asymmetric acetal structure." It is not clear if the compound of the invention requires an asymmetrical structure, or if when the glucocorticosteroid *does* have an acetal structure, it must be an asymmetric one. The claims are thus rendered vague and indefinite.

Regarding claim 10, the limitation "the suspension" lacks adequate antecedent basis.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by O'NEILL (US 3,962,430).

O'NEILL discloses a sterile, aqueous suspension (8 mg/ml) of dexamethasone acetate for parenteral administration. The suspension is prepared using dexamethasone acetate as a micro-fine solid so that 90% of it is below 10 μm. See example 2.

This reference does not disclose a sterile, dry solid, as recited in the claim from which these claims depend. However, when a sterile solution/suspension of the glucocorticosteroid is prepared and sterilized, it is indistinguishable from one prepared from a sterile, dry solid. (See also, discussion of improper dependency in the section bridging pages 2 and 3 of this action.)

Claims 10 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by SAIDI et al (US 6,241,969).

SAIDI teaches sterile solutions of (gluco)corticosteroids, (0.028 to 0.42 mg/ml) including budesonide. See examples.

This reference does not disclose a sterile, dry solid as recited in the claim from which these claims depend. However, when a sterile solution/suspension of the glucocorticosteroid is prepared and sterilized, it is indistinguishable from one prepared from a sterile, dry solid. (See also, discussion of improper dependency in the section bridging pages 2 and 3 of this action.)

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 4, 6, 8-10, 12, 14, 34-36, 39, 41, 42, and 45-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of BUSSEY et al (J. Parenter. Sci. Tech., 1983).

The claims are drawn to a glucocorticosteroid in the form of sterile, dry finely divided particles. Dependent claims recite limitations regarding particle size, purity, and the preparation of pharmaceutical compositions using the sterile glucocorticosteroid.

JAKUPOVIC teaches a crystalline form of the anti-inflammatory agent, budesonide, in which 90% of the particles have a diameter of less than 5.7 μm, for nasal inhalation in treating diseases of the respiratory tract. See example 1, page 8 and page 4, lines 4-6. The reference further teaches a particle range of about 0.1 μm to about 10 μm. See paragraph bridging pages 3 and 4. The reference also teaches the use of other glucocorticosteroids, such as rofleponide and mometasone. The reference further teaches the preparation of pharmaceutical compositions by adding any of a variety of pharmaceutically acceptable carriers. See page 5, beginning line 11, continuing through page 6, line 17.

JAKUPOVIC does not teach a sterile, dry powder. The reference further does not teach the percentage by weight of the glucocorticosteroid.

BUSSEY teaches the sterilization of (gluco)corticosteroid powders by ^{60}Co irradiation. See entire reference, particularly the abstract. The claim also teaches that ethylene oxide is used to sterilize bulk steroids. See introduction.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the respirable, dry powders disclosed by JAKUPOVIC by either irradiation or treatment with ethylene oxide. The artisan would have been motivated to sterilize the respirable particles to prevent microbial growth in the packaged material. The artisan would be particularly motivated to sterilize the glucocorticosteroid in the form which it is intended to be used.

It would also be obvious to the ordinarily skilled worker to purify the glucocorticosteroid (prepare in a form having a high percentage of the glucocorticosteroid by weight) in order to limit contaminants in products for human administration.

It would be further obvious to prepare pharmaceutical compositions for their art-disclosed utility, as described by JAKUPOVIC.

Regarding claims 39, 41, 42, 45, and 46: Claim 39 recites a product-by-process. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. There does not appear to be any difference between a dry glucocorticosteroid sterilized by heating, as recited in the claims, and a dry glucocorticosteroid sterilized by irradiation or treatment by ethylene oxide.

Claims 3, 4, 6, 8-10, 12, 14, 32-37, 39-42, and 45-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of BUSSEY et al (J. Parenter. Sci. Tech., 1983) and in further view of RADHAKRISHNAN et al (US 5,192,528).

The invention is as set forth above. Dependent claims further limit the particle size.

JAKUPOVIC teaches as set forth above. The aim of the reference is preparation of glucocorticosteroids available to the lower respiratory tract. See page 1, lines 9-15. As noted above, JAKUPOVIC teaches the range of particles of about 0.1 μm to about 10 μm, but the reference does not specifically exemplify particles of less than 5 μm.

BUSSEY teaches as set forth above.

RADHAKRISHNAN teaches that aerosol particles must be must be less than about 1 μm in order to reach the lower region of the respiratory tract (alveoli). See figure 1 and col 5, lines 37-48.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare respirable particles of less than 1 μm. The artisan would have been motivated to prepare this size in order for the respirable glucocorticosteroid to reach the alveoli during treatment with a reasonable expectation of success.

Claims 3, 4, 6, 8-12, 14, 30, 31, 34-36, 38, 39, 41-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) in view of BUSSEY et al (J. Parenter. Sci. Tech., 1983) and in further view of SEQUIEIRA et al (US 5,837,699).

The invention is as set forth above. Dependent claims recite methods of treating specific respiratory disorders by administering the sterile glucocorticosteroid and concentrations of the pharmaceutical compositions comprising the sterile glucocorticosteroid.

JAKUPOVIC teaches as set forth above. The reference teaches treatment of diseases of the respiratory tract in general, but not the particular disorders recited in the claims.

BUSSEY teaches as set forth above.

SEQUIEIRA teaches nasal inhalation of a number of (gluco)corticosteroids including budesonide and mometasone for the treatment of specific respiratory disorders, such as COPD, asthma, and rhinitis. See col 1-2. The reference further teaches administration of the

glucocorticosteroid as a dry powder or as an aqueous suspensions of about 0.01 to about 10 mg of glucocorticosteroid to gram of suspenstion. See col 5. Given that 1g water = 1ml water, this range is approximately the same as the concentrations (mg/ml) recited in the claims.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the dry, sterile glucocorticosteroids or as aqueous suspensions of said glucocorticosteroids for the treatment of the recited respiratory disorders for their art-disclosed utility. It would be within the scope of the artisan to optimize the dosage through routine experimentation.

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over RADHAKRISHNAN et al (US 5,192,528).

The invention is as set forth above.

RADHAKRISHNAN teaches liposomal compositions of glucocoticosteroid, (about 0.1 to about 2 mg/ml) including budesonide. Beclomethasone is exemplified. See examples. The reference teaches that the liposomal preparations can be sterilized by filtration, but a sterilized composition is not specifically exemplified. See col 6, lines 13-17.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the liposomal solution by filtration. The artisan would have been motivated to sterilize the solution to prevent microbial growth in the pharmaceutical preparation.

This reference does not disclose a sterile, dry solid. However, when a sterile solution/suspension of the glucocorticosteroid is prepared and sterilized, it is indistinguishable from one prepared from a sterile, dry solid.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Tuesday, Wednesday, or Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Gary Geist (703) 308-1701, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

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Leigh C. Maier
Patent Examiner
March 8, 2002